



TO **the Chairman** of the Scientific Jury, **appointed** at the  
First Meeting of the Scientific Jury of 11.08.2025 on the  
occasion of Order No. **P-109-332 / 28.07.2025 of the**  
Rector of the Medical University of Varna

## OPINION

**SUBJECT:** Dissertation for **the acquisition of the educational and scientific degree "Doctor"** by Dr. Yavor Anzhelov Petrov, doctoral student at the Second Department of Internal Medicine, Faculty of Medicine, Medical University - Varna, on the topic *"Role of lymphocyte populations after allogeneic transplantation of hematopoietic stem cells"* in the field of higher education 7. Health and Sports, professional field 7.1. Medicine and **doctoral program "Hematology and Blood Transfusion"**, with scientific supervisor Prof. Dr. Ilina Dimitrova Micheva, MD, PhD - Second Department of Internal Medicine, Medical University - Varna.

**PREPARED BY:** **Assoc. Prof. Dr. Trifon Georgiev Chervenkov, MD, PhD**, Associate Professor of Clinical Immunology at the Department of Medical Genetics, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna, *Member of the Scientific Jury* according to Order No. **P-109-332 / 28.07.2025 of the** Rector of the Medical University - Varna and appointed as *Chairman of the Scientific Jury and internal member, preparing the opinion* according to Protocol No. 1 of 11.08.2025 of the First Absentee Meeting of the Scientific **Jury**.

### **I. General data about the dissertation work of Dr. Yavor Petrov.**

The dissertation work of Dr. Yavor Petrov extends over 105 standard printed pages. The text is divided into introduction, literature review, aim and objectives, materials and methods, results, discussion, conclusions, contributions, conclusion, publications, bibliography. The data obtained and the analyses performed are illustrated with 19 tables and 52 figures. The bibliography contains 386 titles, all of which are by foreign authors.



## **II. Assessment of the relevance of the topic**

Allogeneic hematopoietic stem cell transplantation is the therapy of choice for a number of malignant hematological diseases, and immune recovery after transplantation is a critical factor for infectious morbidity, GVHD and overall survival. The dissertation is focused on the dynamics of lymphocyte subpopulations and the factors that modify it, which is of direct clinical relevance.

## **III. Evaluation of the literature review**

The literature review is extremely comprehensive and introduces the reader to the issues of the dissertation. In practice, the literature review is spread over several subchapters of the dissertation. The author successively presents a historical overview of allo-SCT, technical aspects of allo-SCT, complications related to transplantation, immune recovery after HSC transplantation. The volume of the literature review is optimal and occupies about 1/3 of the dissertation. work and prepares the reader for the research questions and methodology.

## **IV. Evaluation of the set goals and objectives**

The main goal of the dissertation is clearly formulated. The aim of the present work is to analyze the absolute lymphocyte count and lymphocyte subpopulations in patients with malignant hematological diseases after allogeneic hematopoietic stem cell transplantation and their correlation with various transplantation factors and complications. For the given goal, the five tasks formulated are directly related to the implementation of the goal, and the goal is feasible.

## **V. Evaluation of the methods used**

The methods used in the dissertation study are presented in the fifth chapter, in separate subchapters for the studied patient group, donors and type of graft, conditioning regimens and immunosuppression, flow cytometric analysis of lymphocyte subpopulations. Statistical methods U -test were used. Mann –Whitney, ANOVA+Tukey, Spearman,  $\chi^2$ , linear / logistic regression, ROC analysis (AUC, 95% CI).



The contingent and laboratory methods are described in detail and each of the laboratory tests can be repeated without the need for additional information.

## VI. Evaluation of the presented results

The results are presented in the sixth chapter, illustrated with convincingly presented tables and graphs of the results. The results are summarized as follows: overall recovery: ALC shows an increasing trend until day +180; on day +100 representative values are observed: CD4 ~480 cells/ $\mu$ l; NK ~135 cells/ $\mu$ l; CD19 ~67 cells/ $\mu$ l; transplantation factors: best recovery in a related donor; most delayed – in haploidentical donors; better indicators in male donors at separate time points. FluBu and ATG are associated with lower CD4 (day +100) and suppressed NK (day +180/+270); complications: GVHD, infections, relapse, etc. show a negative relationship with the number of NK and CD19+ cells; ROC and threshold values: clinically applicable thresholds for day +100/+180 are determined: CD4 375/284 cells/ $\mu$ l; CD8+CD38+ 532/284 cells/ $\mu$ l; NK 128/112 cells/ $\mu$ l; CD19 66/49 cells/ $\mu$ l; ALC  $1.04/1.07 \times 10^9/l$ : below these thresholds survival is significantly lower. I accept that so the presented results support the conclusions.

## VI. Evaluation of the contributions of the dissertation

The contributions of this dissertation are as follows: original – first in our country assessment of the influence of transplantation factors on the recovery of lymphocyte subpopulations ; first in our country assessment of the relationship between complications (GVHD/infections) and immune recovery; first in our country analysis of the relationship between lymphocyte recovery and overall survival after allo-SCT; scientific and practical: validated cut-off values for key subpopulations on day +100/+180 with prognostic value; argument for routine immunomonitoring and personalized modification of immunosuppression /maintenance therapy and confirmatory: diagnosis, donor type and conditioning affect immune recovery; complications worsen it; unsatisfactory recovery compromises long-term survival.

I consider the contributions sufficient to acquire the ONS "Doctor".



### **Conclusion**

The presented dissertation work of Dr. Yavor Anzhelov Petrov is significant, methodologically correct and with clear clinical implications. In my opinion, this is a stable scientific work and meets the requirements of the ZRAS of the Republic of Bulgaria and the RAS Regulations of the Medical University - Varna for acquiring the ONS "Doctor" and I give my positive assessment for awarding the scientific and educational degree "Doctor" in the field of higher education 7. "Healthcare and Sports", professional direction 7.1. Medicine in the scientific specialty "Hematology and Blood Transfusion" to Dr. Yavor Anzhelov Petrov.

Заличено на основание чл. 5,  
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/ Assoc. Dr. Trifon Chervenkov, Ph.D./